II. REMARKS

Preliminary Remarks

Reconsideration and allowance of the present application based on the following remarks are respectfully requested. Claims 1-31 are currently pending in this application and remain at issue. This response is timely filed as it is accompanied by a petition for an extension of time to file in the first month and the requisite fee.

On page 2 of the official action, the examiner objected to claims 4, 10-24, and 26-31 under 37 C.F.R. §1.75(c) as being in improper form due to multiple dependent claims depending from other multiple dependent claims. The applicants submit that the multiple dependencies have been removed from claims 4 and 10-24, and 26-31 as set forth above. In view of the foregoing amendment, the applicants respectfully request that the objection to claims 4, 10-24 and 26-31 has been overcome, and should now be removed.

On pages 2 and 3 of the official action, the examiner objected to claim 25 under 37 C.F.R. §1.75(c) has being an improper dependent claim because it failed to limit the subject matter of the previous claim. Amended claim 25 is directed to a polymer modified biological element obtainable by the process according to claim 24 and thus overcomes the typographical error. In view of the foregoing amendment and remarks, the applicant respectfully requests that the objection to claim 25 has been overcome, and should now be examined on the merits.

New claim 32 is directed to a method according to claim 1, wherein the synthetic hydrophilic multivalent polymer comprises a polymer backbone based upon monomer units selected from the group consisting of N-2-hydroxypropylmethylacrylamide (HPMA), N-(2-hydroxyethyl)-1-glutamine (HEG), ethyleneglycol-oligopeptide, or dextran. Support for new claim 32 can be found throughout the specification, for example, on page 6, lines 25 to 30 as well as the content of WO 98/19710, which is included in the applicants' invention by reference.

New claim 33 is directed to a polymer modified biological element as claimed in Claim 21 wherein the biological element is an adenovirus. Support for new claim 33 can be found throughout the specification, for example, on page 13, lines 18-21 and Example 4. The applicants do not intend by these or any amendments to abandon subject matter of the claims

as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications.

Patentability Remarks

Rejection Pursuant to 35 U.S.C. §112, First Paragraph

Written Description

On pages 3-5 of the official action, the examiner rejected claims 1-3, and 5-9 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. Specifically, the examiner asserted that these claims encompass a broad genus of multivalent polymers that include any multivalent polymer of any type. The examiner further alleged that these multivalent polymers retain the function of forming a complex with any type of bacterial cell, viral particle, bacteriophage, or spore wherein the multivalent polymer forms at least two covalent linkages and alters at least one biological or physiochemical property of the biological element. The examiner further asserted that the specification teaches only two working examples around multivalent polymers having an N-2-hydroxypropylmethylacrylamide (hereafter "HPMA"), N-(2-hydroxyethyl)-1-glutamine (hereafter "HEG"), or ethylenglycol-oligopeptide backbone. The examiner finally alleged that no additional multivalent polymer that form multiple covalent linkages per polymer molecule to modify biological properties of a bacterial cell, viral particle, bacteriophage or spore are described in the specification or in the prior art. The examiner concluded that given the enormous genus of multivalent polymerse, the lack of description in the specification or prior art of other embodiments of such multivalent polymers, one of skill would reasonably conclude that the applicants were not in possession of the broadly claimed invention.

Amended claim 1 is directed to a method of modifying the biological and/or physicochemical properties of a biological element, said method comprising reacting said biological element with a synthetic hydrophilic multivalent polymer having multiple reactive groups wherein the biological element is linked to the polymer by a plurality of linkages. Amended claim 6 is directed to a polymer modified biological element in which the biological element is covalently linked to a synthetic hydrophilic multivalent polymer having multiple reactive groups wherein said polymer is linked to the biological element by at least two covalent linkages. Support for amended claims 1 and 6 can be found throughout the specification, for example, on page 6, lines 13-15. The applicants respectfully submit that

examples of a number of the synthetic hydrophilic mulivalent polymer backbones (*i.e.*, HPMA, HEG and ethyleneglycol-oligopeptide) are fully described in specification for example, on page 6, lines 30-35 and Example 1. The applicants submit that the description of the examples using HPMA, HEG, and PEG provide sufficient guidance to other suitable polymers. One of skill in the art will know the chemical nature of the groups present on the surface of a biological element to couple with synthetic hydrophilic polymers. Using his knowledge of chemistry regarding reacting the polymer, one of skill can choose the necessary hydrophilic group required to be present on the polymer in order to transform the hydrophilic polymer into reactive groups which complement the surface of the biological element. Therefore, given the constraints on the system in terms of complementary reactive groups between the polymer and the biological element, one of skill, reading the description of the application, would be able to identify a limited number of suitable hydrophilic multivalent polymers for manipulation. Thus, the applicants submit that they were in possession of the broadly claimed invention at the time of filing.

Dependent claims 2, 3, and 5-9 depend from and contain the same limitation as amended claim 1 or 6. Similarly, objected claims 4 and 10-34 depend from and contain the same limitation. In view of the foregoing remarks and amendment, the applicants submit that the rejection of claims 1-3 and 5-9 under 35 U.S.C. §112, first paragraph, for lack of written description has been overcome, and a rejection of amended claims 4, and 10-33 would be improper.

Enablement

On pages 5-8 of the official action, the examiner rejected claims 1-3 and 5-9 under 35 U.S.C. §112, first paragraph, for allegedly lacking enablement. Specifically, the examiner asserted that while the embodiments of a multivalent polymer backbone consisting of either HPMA, HEG, or ethyleneglycol-oligopeptide are enabled by the specification, the specification does not provide a sufficient enabling disclosure wherein the mulivalent polymer is derived from a different polymer backbone. The examiner asserted that the nature of the invention is complex involving covalent attachment of a single polymeric molecule to at least two sites on the surface of an altered biological element (*e.g.*, phage, virus, or bacterial cell). The examiner alleged that the breadth of the claims encompass a large number of multivalent polymers linked to these altered biological elements. The examiner further asserted that there is no significant guidance of other multivalent polymers wherein

the backbone is not derived from HPMA, HEG, or ethyleneglycol-oligopeptide. The examiner alleged that using multivalent polymers to generate altered biological elements through multiple covalent linkages per polymer is novel in the art. The examiner cited WO 98/44143 as prior art that fails to provide further guidance with regard to adapting other types of polymer backbones for use in attaching biological elements to multivalent polymers with at least two covalent bonds.[1] The examiner concluded that due to these factors, one of skill in the art would have to perform undue trial and error experimentation to develop other types of multivalent polymers to practice the claimed invention.

The applicants submits that the specification (and its teachings) clearly enables one of skill in the art to identify other hydrophilic multivalent polymer backbones other than HPMA, HEG, and ethyleneglycol-oligopeptide. The polymer backbone must be hydrophilic. The reactive groups that make up the hydrophilic backbone must complement those surface reactive groups on the surface of the biological element. The options available to one of skill in the art is limited to a finite number of combinations. The examples teach that using HPMA, HEG, and PEG demonstrate the types of reactive groups are required suitable for the polymer to form a linkage on the surface of the biological element. One of skill has this knowledge of this type of chemistry based upon the teachings of the specification. For example, the applicants submits that the fully included reference WO 98/19710 refers to the use of dextran as a hydrophilic multivalent polymer (see Example 17 of WO 98/19710). In addition to the disclosed examples of HPMA, HEG, and PEG, polysaccherides such as dextran could be identified by one of skill in the art to be a suitable hydrophilic multivalent polymer for reacting with particular surface molecules of a biological element. Accordingly, one of skill is initially directed to a particular area of suitable multivalent hydrophilic multivalent polymers for manipulation such that undue trial and error experimentation is not necessary.

As discussed above, dependent claims 2, 3, and 5-9 depend from and contain the same limitation as amended claim 1 or 6. Similarly, objected claims 4 and 10-34 depend from and contain the same limitation. In view of the foregoing remarks and amendment, the applicant submits that the rejection of claims 1-3 and 5-9 under 35 U.S.C. §112, first paragraph, for

[1] The examiner asserted that WO 98/44143 only teaches modifying a virus particle through a single covalent linkage with polyethylene glycol (PEG).

lack of enablement has been overcome, and a rejection of amended claims 4, and 10-34 would be improper.

Rejection Pursuant to 35 U.S.C. §112, Second Paragraph, Indefiniteness

On page 8 of the official action, the examiner rejected claims 1-3 and 5 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Specifically, the examiner asserted that claim 1 was unclear with regard to the phrasing "change or modify" because it appeared to him as being synonymous. The examiner further alleged that claim 3 was unclear for the phrasing "such as" because it was unclear whether the limitation following this phrase are a necessary part of the claim.

The applicant submits that terms change or modify have been removed from claim 1. The applicant further submits that the term "such as" has been replaced with the term "wherein" in claims 1 and 3 to more clearly indicate the phrase following the term "wherein" is a necessary part of the claim. Claim 2 depends from and contains the same limitation as claim 1. Claim 5 draws its dependency from claim 3 and thus contains the same limitations. In view of the foregoing remarks and amendment, the applicant submits that the rejection of claims 1-3 and 5 have been overcome and should be withdrawn.

III. CONCLUSION

In view of the foregoing, the applicant submits that they have fully and properly responded to the outstanding restriction requirement. Should the examiner have any questions or comments regarding this response or the application, the examiner is urged to contact the undersigned at the number indicated.

Respectfully submitted,

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